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SHORT COMMUNICATION

Treatment adherence and patients' acceptance of home infusions with adenosine 5′-triphosphate (ATP) in palliative home care

Sandra Beijer · Nicole E. G. Wijckmans · Erik van Rossum · Cor Spreeuwenberg · Ron A. G. Winkens · Lisette Ars · Pieter C. Dagnelie

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Abstract
Goals of work In preterminal cancer patients, provision of palliative care in the patients' own environment is preferred. The aim of the present study was to evaluate patients' and caregivers' treatment adherence and patients' acceptance of home infusions with adenosine 5′-triphosphate (ATP).
Patients and methods Preterminal cancer patients (life expectancy <6 months) with mixed tumor types were eligible for the study. Patients received a maximum of eight weekly intravenous 8–10 h ATP infusions. Evaluation of treatment adherence was based on registration of protocol deviations and patients' acceptance by structured interviews with patients.
Main results Fifty-one patients received a total of 266 intravenous ATP infusions. The infusion protocol was well executed: mean duration ≈8.30 h, stepwise achievement of the maximum infusion rate within 30 min in 65% of the infusions, and almost no delay in weekly administration. All except one patient were not burdened by the administration of the infusions at home and none of them had felt afraid. The majority of patients found the advantages of the ATP infusions outweighing the disadvantages. However, an important bottleneck in the administration of ATP infusions at home was difficulty in establishing venous access.
Conclusion ATP infusions at home are well accepted by patients. Difficulties in establishing venous access might be reduced by composing specialized home infusion teams working both at the day care center and at home or by adopting an alternative route of venous access.

Keywords ATP · Treatment adherence · Home infusion · Palliative care

S. Beijer (✉) · N. E. G. Wijckmans · P. C. Dagnelie
Department of Epidemiology, NUTRIM, Maastricht University,
P.O. Box 616, 6200 MD Maastricht, The Netherlands
e-mail: sandra.beijer@epid.unimaas.nl

E. van Rossum · C. Spreeuwenberg
Department of Health Care Studies, Maastricht University,
P.O. Box 616, 6200 MD Maastricht, The Netherlands

E. van Rossum
Center of Expertise on Autonomy and Participation,
University Zuyd,
Heerlen, The Netherlands

R. A. G. Winkens
Department of Integrated Care, University Hospital Maastricht,
P.O. Box 5800, 6202 AZ Maastricht, The Netherlands

R. A. G. Winkens
Department of General Practice, Maastricht University,
P.O. Box 616, 6200 MD Maastricht, The Netherlands

L. Ars
Home Care Organization,
Groenekruis Domicura Maastricht and area,
Mockstraat 1, 6226 CA Maastricht, The Netherlands

Introduction

Over the past 15 to 20 years, a major change in the delivery of health care has occurred. Increasing numbers of patients suffering from different diseases receive intravenous therapy at home including intravenous antibiotics, steroids, biphosphonates, and parenteral nutrition [8–11, 14, 17, 19, 20]. Also in cancer care, home administration of intravenous medication (chemotherapy, opiates) is becoming a widely used alternative to treatment in hospital [7, 14, 17]. Especially

in terminally ill cancer patients, it is preferred to provide palliative care in their own environment [18, 19].

A potential agent in palliative care is adenosine 5′-triphosphate (ATP). A randomized clinical trial in patients with advanced non-small cell lung cancer [3, 4] showed that ATP infusions had marked favorable effects on body weight, muscle strength, fatigue, nutritional intake, quality of life, and survival [1, 3, 4].

Unfortunately, ATP cannot be given by alternative routes of administration like oral application or hypodermoclysis. In studies published so far, ATP infusions were given in a clinical setting. However, several authors [2, 12, 13] have reported that continuous application of low-dose ATP is generally safe. Dyspnea, chest discomfort, and the urge to take a deep breath were the most common side effects; all side effects were mild and transient, resolving within minutes after lowering the ATP dose. No symptoms of cardiac ischemia occurred in any of the infusions [2, 5]. Because of the favorable safety profile of ATP and to diminish the burden on the patients, we decided to administer ATP at the patient's home. The aim of the present study was to evaluate patients' and caregivers' treatment adherence to the ATP infusion protocol and patients' acceptance of ATP infusions at home.

Patients and methods

Patients

Patients were recruited through the Departments of Medical Oncology and Pulmonology of five hospitals in the southern half of The Netherlands (located in Maastricht, Eindhoven, Utrecht, and Heerlen) and through 50 general practitioners in the region of Maastricht. Eligible for the study were patients with cytologically or histologically confirmed cancer, for whom medical treatment options were restricted to supportive care, who had a life expectancy <6 months, and had a World Health Organization (WHO) performance status 1 or 2. Since the present study was part of a randomized clinical trial aiming to study the effects of ATP on nutritional status and fatigue, eligible patients also had to suffer from at least one of the following complaints: fatigue, anorexia, or weight loss >5% over the previous 6 months. Excluded were patients with symptomatic angina pectoris, symptomatic heart failure, or any form of atrioventricular block (assessed by electrocardiogram), life expectancy <4 weeks, concurrent palliative chemotherapy, and cognitive dysfunction. After baseline measurements, patients were randomly allocated to ATP or control treatment, using computer-generated random numbers with permutation blocks of four. One hundred patients were randomly assigned to the ATP (n=51) or control (n=49) group. The present report on treatment adherence and patients' acceptance of ATP administration at home is restricted to all 51 patients randomized to ATP treatment. Baseline characteristics of ATP-treated patients are shown in Table 1. The study was approved by the Ethical Committees of all hospitals involved in the study, and all patients signed written informed consent prior to the study. Details of the trial design have been published elsewhere [6].

Treatment protocol

Over a period of 8 weeks, patients received eight ATP courses of 8–10 h each, at weekly intervals. To prevent side effects, all ATP infusions started beginning at a dose of 20 mcg/kg.min and were increased in steps of 10 mcg/kg.min every 10 min until a maximum dose of 50 mcg/kg.min, or in case of side effects, until the maximally tolerated dose (MTD) had been reached. Thereafter, ATP was infused at a constant rate. Since initiation of ATP infusions under medical supervision in a clinical setting would facilitate the treatment of possible side effects, the first two ATP infusions were given at the day care center of the participating hospitals. Based on the mild character of the noted side effects during the first two infusions in the first 22 patients, in order to minimize hospitalization of these preterminal patients, an amendment was granted by the Ethical Committee during the study for administering only the first ATP infusion at the day care center. All subsequent infusions were administered at home by experienced, highly qualified, and trained nurses of the infusion team of the regional Home Care Organization or hospital. Eligibility for home infusion therapy was checked using specific criteria (Table 2). Patients and their informal

Table 1 Baseline characteristics of ATP-treated patients (n=51)

	Number	Percent
Age (years)	68.1 (45–87)[b]	
Gender		
Male	35	69
Female	16	31
WHO performance score[a]		
1	33	65
2	18	35
Tumor type		
Lung	21	41
Colon	8	16
Gastrointestinal other	6	12
Prostate	5	10
Other	11	21

[a] WHO 1—restricted in physically strenuous activity but ambulatory and able to do light work; WHO 2—ambulatory (not more than 50% in bed) and capable of self-care but unable to carry out any work

[b] Mean (range)

Table 2 Eligibility criteria for home infusion therapy

Appropriate housing situation and sanitary conditions
Telephone or comparable device for external communication
Presence of informal caregiver in the home
Psychological ability of patient and family to cope with the potential stress of home infusions
Motivation of patient and informal care giver for home infusions
Acceptance of responsibility for the home infusions, i.e., to report side effects and/or to stop the infusion in case this would be needed

caregivers were instructed in detail on the infusion procedures and to call the infusion team in case of side effects or any other problems. All participating nurses received special instructions (verbal and written) on how to administer, increase, and end the ATP infusions; what to do in case of side effects; which items had to be checked and reported; and how to instruct the patient and/or informal caregiver.

Data collection and analysis

Patients' adherence was evaluated by registering the number of patients who stopped with the ATP infusions before the end of the study and the reasons for drop out. Patients' acceptance was investigated by structured interviews after four and eight infusions. Only the latest available evaluation was processed for the present paper. These interviews included questions about burden, duration, frequency, and perceived benefits and disadvantages of the infusions as well as feelings of anxiety during the infusions. Adherence to the treatment protocol was evaluated by standardized registration of the course of the infusions and all protocol deviations. All data were analyzed in a descriptive way using SPSS 13.0 for Windows.

Results

Patients' adherence to ATP administration

Of the 51 included patients, 6% did not start with ATP infusions, 29% received one to three courses, 18% four to seven courses, and 47% completed all eight infusions (Fig. 1). Twelve patients decided to continue ATP administration after completion of the eight regular infusions.

Six patients died during the intervention period. Twenty-one patients stopped or did not start with ATP infusions for reasons of deterioration in medical condition (n=14), fear of side effects (n=4), or being unsatisfied with the effect of the ATP (n=3).

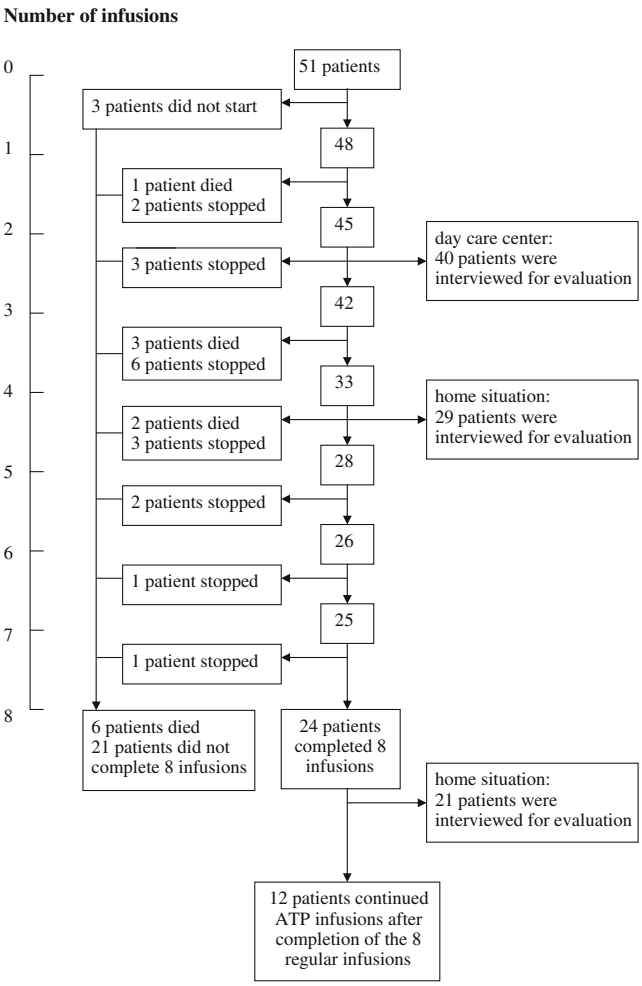

Fig. 1 Flow diagram of the study

Acceptance by patients

Twenty-nine patients (57% of total) were interviewed about their experiences with ATP infusions at home. Twenty-two patients were not assessable because of death or deterioration in medical condition. All except one patient were not burdened by the home infusions. Patients mentioned that it was more relaxed at home and that it was possible to continue daily activities in one's own environment. The infusion frequency of once a week was evaluated as "good" by 25 patients. The duration of 8–10 h was experienced as too long by 11 patients, although many patients added that they accepted the infusion duration that was perceived necessary for obtaining maximal results. None of the patients had felt afraid during the home infusions. Twenty-one patients found the advantages of the ATP infusions outweighing the disadvantages. Main disadvantages of home infusions mentioned by patients were problems with establishing venous access, restriction of daily activities by the infusion, and burden for the informal caregiver.

Protocol adherence

A summary of protocol deviations is given in Table 3. Of the 408 planned ATP infusions, 142 infusions were not administered due to deterioration of medical condition or death.

Of the 266 infusions given, 95 infusions (36%) were administered at the day care center of the participating hospitals and 171 infusions (64%) at home. In eight patients, more than two infusions were given at the day care center. Reasons for this were, among other things, fear of side effects or the unavailability of an informal caregiver.

The mean duration of the ATP infusions at home was 8 h 33 min (standard deviation (SD) 1 h 35 min). The mean period to reach the MTD amounted to 27 min at home. According to the study protocol, nurses were to stay with the patient for 30 min after reaching the MTD. The total spent time was ≈1 h at the start of each infusion and ≈0.5 h at the end of each infusion. In 22 out of 266 infusions, the home nurse had been called during the infusion and had to visit the patient to solve the problems (side effects, infusion pump alarm, etc.), implicating an additional time investment varying from 30–90 min.

Discussion

The objective of this study was to evaluate treatment adherence and patients' acceptance of ATP infusions at home in patients with preterminal cancer. As far as we know, this is the first study in which ATP infusions have been systematically administered at home. Results show that the administration of the infusions was largely carried out according to protocol: mean duration ≈8.30 h, stepwise achievement of the maximum infusion rate within 30 minutes in 65% of the infusions, and almost no delay in weekly administration.

However, an important bottleneck in the administration of ATP infusions at home was difficulty in establishing venous access, possibly due to the history of chemotherapy in many patients. As far as we know, little is written about this problem in the literature. In most studies, venous access devices (Port-a-cath, peripherally inserted central catheter (PICC), or peripheral venous cannula) were inserted during hospital stay or at the day care unit and left in place when the patient went home [8, 14, 17, 20]. In our study, the peripheral venous cannula had to be inserted at home by the home nurse of the infusion team. Lapostolle et al. [15] reported a study on a total of 671 attempts to obtain peripheral intravenous access in 495 patients in emergency care in out-of-hospital settings. The first attempt was successful in 368 cases (74%) and unsuccessful in 127 (26%). Peripheral intravenous access was finally achieved in 99% of the patients. Improved success rate was reported when attempts were performed by a nurse specialized in emergency care in patients without a particular medical history like chemotherapy, diabetes, or previous multiple hospitalizations. Initial teaching and regular practice significantly increased the success rate [15].

Table 3 Protocol and deviations from protocol

	Protocol	Actual performance of ATP administration	
Number of infusions	408 infusions planned (8 infusions×51 patients)	266 infusions administered	
		0 infusions	3 patients (6%)
		1–3 infusions	15 patients (29%)
		4–7 infusions	9 patients (18%)
		8 infusions	24 patients (47%)
Mean duration of infusions	8–10 h	Day care center	8 h 05 min±0 h 49 min (mean±SD)
		At home	8 h 33 min±1 h 35 min
Run in period	30–45 min	<30 min	172 infusions (65%)
		30–45 min	55 infusions (21%)
		>45 min	27 infusions (10%)
		Unknown	12 infusions (5%)
Frequency	Once per week	Once per week	263 infusions
		Delayed for 14 days	3 infusions
Day care center: 95 infusions (36%)	First two infusions	First infusion	25
		First two infusions	15
At home: 171 infusions (64%)		More than two infusions	8
Establishing venous access at home	Home infusion nurses	Home infusion nurses	137 infusions (80%)
		Day care center	25 infusions (15%)
		Ambulance personnel	6 infusions (4%)
		Hospital nurse at home	3 infusions (2%)

In our study, one of our participating centers solved the problem of difficulties in establishing venous access by a transmural infusion team composed of trained infusion nurses working both at the hospital and in the home situation, thus providing regular practice in inserting infusion needles. Another solution would be to choose an alternative route of venous access. In the present study, a PICC was successfully inserted in one patient.

Our finding that most patients and informal caregivers preferred home infusions is in accordance with other studies. A study comparing hospital and home antibiotic treatment for cellulitis showed that home care is the preferred treatment choice by patients, particularly for those patients who have experienced community care before [9]. In patients with colon cancer receiving chemotherapy, global patient satisfaction with health care was greater in patients receiving home chemotherapy than in patients receiving outpatient treatment [7]. In a study in patients with Fabry disease [16], most patients also preferred treatment at home.

A considerable proportion of patients (38%) perceived the duration of the infusions at home as too long. Further investigations are warranted to explore other treatment schedules. Technological development may allow smaller, more mobile, and less noisy infusion pumps, contributing to patient comfort.

No feelings of anxiety were reported by the patients in the present study. Zimran et al. [20] also showed no feelings of fear or anxiety associated with infusion treatment at home. In contrast, study patients participating in a self-administration program in which they had to handle the venous access device themselves [14] did show feelings of uncertainty and anxiety. With regard to the first infusion, our study indicates that patients felt safe when this infusion was administered at the day care center.

This evaluation study has some limitations. Inherent to the study population of preterminal cancer patients is the relatively small proportion of patients who completed all eight infusions. This may have led to selection bias since patients with the worst condition will drop out first, restricting the evaluation to patients with fewer problems and easier-to-administer infusions. Furthermore, for logistic reasons, data for the present study had to be collected by the same researcher who was involved in patient instruction and organization of the infusion protocol. Even though great care was taken to allow patients and caregivers to freely express their opinion and feelings, the possibility of biased information by socially desired answers cannot be completely disregarded.

Despite these limitations, we conclude that patients' and caregivers' adherence to the ATP infusion protocol is high and that ATP infusions at home are well accepted by patients. Possibilities to increase the comfort for the patient would be to perform the infusion during the night. Difficulties in establishing venous access might be reduced by composing specialized home infusion teams working both at the day care center and at home or by adopting an alternative route of venous access.

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